

9
9/13/02
8W

Patent
Attorney's Docket No. 002010-586

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of)

Jing Wu, et al.)

Application No.: 09/916,440 ✓)

Filed: July 30, 2001 ✓)

For: CYCLOALKYL, LACTAM, LACTONE)
AND RELATED COMPOUNDS,)
PHARMACEUTICAL COMPOSITIONS)
COMPRISING SAME, AND METHODS)
FOR INHIBITING β -AMYLOID)
PEPTIDE RELEASE AND/OR ITS)
SYNTHESIS BY USE OF SUCH)
COMPOUNDS ✓)

Group Art Unit: 1624

Examiner: B. Kifle

RECEIVED

SEP 12 2002

TECH CENTER 1600/2900

RECEIVED
TECH CENTER 1600/2900
02 SEP -5 PM 4:34

SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

In accordance with the duty of disclosure as set forth in 37 C.F.R. § 1.56, Applicants hereby submit the following information in conformance with 37 C.F.R. §§ 1.97 and 1.98.

Pursuant to 37 C.F.R. § 1.98, a copy of each of the documents cited below is enclosed.

U.S. Patents

2,938,029	Brenner et al.	5/24/60
3,598,859	Yates et al.	8/10/71
4,080,449	Croisier et al.	3/21/78
09/12/2002 TS4660,000 09/09/021 09916440	Karenwesky	7/17/84
01 FC:126 5,478,857	Clemens et al.	12/26/95
5,658,901	Claremon et al.	8/19/97

(5/00)

No Ref.'s Sent

Foreign Patents

0 061 187	9/29/82	Europe
810221A		Europe
WO 92/16524	10/1/92	PCT
WO 95/25117	9/21/95	PCT
WO 96/25408	8/22/96	PCT
WO 96/29313	9/26/96	PCT
WO 97/38705	10/23/97	PCT
WO 98/04539		PCT
WO 97/16410	5/9/97	PCT
WO 98/22494	5/28/98	PCT
WO 98/22430	5/28/98	PCT
WO 98/22433	5/28/98	PCT
WO 98/22494	5/28/98	PCT
WO 98/38177	9/3/98	PCT
GB 1,519,495	7/26/78	UK
HU 71515B	12/28/95	Hungary (abstract only)
179757		Japan

RECEIVED

SEP 12 2002

TECH CENTER 1600/2900

Non-Patent References

Akhatar, et al., "Bicyclic Imides with Bridgehead Nitrogen..", *J. Org. Chem.*, 55: pp. 5222-5225 (1990).

Armstrong, et al., "An Efficient Asymmetric Synthesis of (R)-3-Amino-2,3,4,5-tetrahydro-1H-[1]benzazepin-2-one", *Tetrahedron Letters*, 35: pp. 3239-3242 (1994).

Barton, et al., "A New Rearrangement of Ketonic Nitrones...", *J. Chem. Soc.*, pp. 1764-1767 (1975).

Ben-Ishai, et al., "Intra vs Intermolecular Amidoalkylation of Aromatics", *Tetrahedron*, 43:2, pp. 439-450 (1987).

Blade-Font, "Facile Synthesis of γ -, δ -, and ϵ -lactams by Cyclodehydration of ω -amino Acids on Alumina or Silica Gel", *Tetrahedron Letters*, 21: 2443-2446 (1980).

Brown, et al., "A Revision of the Structure of "7-Phenyloxindole", *Tetrahedron Letters*, 8: pp. 667-670 (1971).

Burkholder, et al., "The Synthesis of 6-Amino-5-Oxo-7-Phenyl-1,4-Oxazepines As Conformationally Constrained *Cauche* (-) Dipeptide Mimetics", *Biog. Med. Chem. Letter*, 2: p. 231 (1993).

Busacca, et al., "Synthesis of Novel Tetrahydrobenzazepinones", *Tetrahedron Letters*, 33:2, pp. 165-168 (1992).

Butcher, et al., "Preparation of 3-Amino-1,4-Benzodiazepin-2-Ones Via Direct Azidation with Trisyl Azide", *Tetrahedron Letters*, 37:37, pp. 6685-6688 (1996).

Chartier-Harlin, et al., "Early-onset Alzheimer's disease caused by mutations at codon 717 of the β -Amyloid precursor protein gene.", *Nature*. 353:31, pp. 844-846 (1991).

Citron, et al., "Mutation of the β -amyloid precursor protein in familial Alzheimer's disease increases β -amyloid protein production.", *Nature* 360:672-674 (1992).

Clark, et al., "Effects of Remote *N*-(*tert*-Butoxycarbonyl) Groups on Heteroatom Directed Lithiation at Benzylic Positions", *Tetrahedron*, 49:7, pp. 1351-1356 (1993).

Colombo, et al., "Synthesis of 7,5-Fused Bicyclic Lactams by Stereoselective Radical Cyclization", *Tetrahedron Letters*, 35:23, pp. 4031-4034 (1994).

Cornille, et al., "Electrochemical Cyclization of Dipeptides Toward Novel Cyclic, Reverse-Turn Peptidomimetics", *J. Am. Chem. Soc.*, 117: pp. 909-917 (1995).

Crombie, et al., "Transamidation Reactions of β -Lactams", *Tetrahedron Letters*, 27:42, pp. 5151-5154 (1986).

Curran, et al., "A Short synthesis of Bicyclic Dipeptides Corresponding to Xxx-L-Pro and Xxx-D-Pro Having Constrained *Cis*-Proline Amides", *Tetrahedron Letters*, 36, pp. 191-194 (1995).

Das, et al, "Dual Metalloprotease Inhibitors IV", *Biorg. Med. Chem. Lett.*, 4:18, pp. 2193-2198 (1994).

Desai, et al., "Polymer Bound EDC (P-EDC): A convenient Reagent for Formation of An Amide", *Tetrahedron Letters*, 34:48, pp. 7685-7688 (1993).

Dickerman, et al., "Studies in Piperidone Chemistry", *J. Org. Chem.*, 14, p. 530-536 (1949).

Dickerman, et al., "The Schmidt Reaction with 2,2,6-Trimethyl-And 1,3-Dimethyl-4-Piperidones", *J. Org. Chem.*, 20: p. 206-209 (1955).

Dickerman, et al., "The Schmidt Reaction with 3-Ethoxycarbonyl-4-Piperidones and the synthesis of six 5-homo-piperazinones", *J. Org. Chem.*, 19, p. 1855-1861 (1954).

Donaruma, et al., Organic Reactions, Ch. 1, "The Beckmann Rearrangement", pp. 1-156 (1960).

Edwards, et al., "Cyclization and Fragmentation of N-Chloro Lactams", *Can. J. Chem.*, 49: pp. 1648-1658 (1971).

Flynn et al., "Applications of a Conformationally Restricted Phe-Leu Dipeptide Mimetic to the Design of a Combined Inhibitor of Angiotensin I-Converting Enzyme and Neutral Endopeptidase 24.11", *J. Med. Chem.*, 36: pp. 2420-2423 (1993).

Freidinger et al, "Protected Lactam-Bridged Dipeptides for Use as Conformational Constraints in Peptides", *J. Org. Chem*, 47: pp. 104-109 (1982).

Gaetzi, "Fungicidal Amino azacycloheptanones", *Chem. Abs.*, 66: 28690m.

Games, et al., "Alzheimer-type Neuropathology In Transgenic Mice Overexpressing V717F β -amyloid Precursor Protein", *Letters to Nature*, 373: pp. 523-527 (1995).

Glenner, et al. "Alzheimer's Disease: Initial Report of the Purification and Characterization of a Novel Cerebrovascular Amyloid Protein." *Biochem. Biophys. Res. Commun.* 120(3): 885-890 (1984).

Goate, et al. "Segregation of a missense mutation in the amyloid precursor protein gene with familial Alzheimer's disease." *Letters to Nature*. 349: 704-706 (1991)

Gracias, et al., "Efficient Nitrogen Ring-Expansion Process Facilitated by in Situ Hemiketal Formation", *J. Am. Chem. Soc.*, 117: pp. 8047-8048 (1995).

Grunewald, et al., "Effect of Ring Size or an Additional Heteroatom on the Optency and Selectivity of Bicyclic Benzylamine-Type Inhibitors of Phenylethanolamine *N*-Methyltransferase", *J. Med. Chem.*, 39, pp. 3539 (1996).

Hansen, et al., "Re-examination and further Development of a Precise and Rapid Dye Method for Measuring Cell Growth", *J. Immun. Meth.*, 119: pp. 203-210 (1989).

Hart, et al., "The Ester Enolate-Imine Condensation Route to β -Lactams", *Chem. Rev.*, 89: pp. 1447-1465 (1989).

Herschmann, "Recherches sur la nature du Methonitrile de Wallach", *Helv. Chim. Acta*, 7:329, p. 2537-2547 (1949).

Hoffman, et al., "Efficient Synthesis of *N*-Substituted Lactams from (*N*-Arylsulfonyloxy) Amines and Cyclic Ketones", *Tetrahedron Letters*, 30: pp. 4207-4210 (1989).

Hoffman, et al., "Synthesis and Structure of 7-Methyl-and 7-Pheynl-1,2,3,4-Tetrahydro-1,4-Diazepin-5-ones", *Tetrahydrodiazepinones.*, 27: p. 3565 (1962).

Holladay, et al., "Synthesis of α -Benzyl γ -Lactam, α -Benzyl δ -Lactam and α -Benzylproline Derivatives as Conformationally Restricted Analogues of Phenylalaninamide", *J. Org. Chem.*, 56: 3900-3905 (1991).

Hu, et al., "Two Efficient Syntheses of (+)-*anti*-*N*-Benzyl-3-Amino-4-Hydroxyhexahydroazepine", *Tetrahedron Letters*, 36:21, pp. 3659-3662 (1995).

Itoh, K., "Synthesis and Antiotensin Converting Enzyme-Inhibitory Activity of 1,5-benzothiazine...", *Chemical Abstracts*, Vol. 111, No. 15, 10/9/89, Columbus, OH, Astract No. 126464h.

Johnson-Wood, et al. "Amyloid precursor protein processing and A β ₄₂ deposition in a transgenic mouse model of Alzheimer's disease." *PNAS USA*. 94: 1550-1555 (1997).

Kawase, et al., "Electrophilic Aromatic Substituion with *N*-Methoxy-*N*-Acylnitrenium Ions Generated from *N*-Chloro-*N*-Methoxyamies", *J. Org. Chem.*, 54: pp. 3394-3403 (1989).

King, et al., "Iodotrimthylsilane-Mediated 2-Mononhalogenation of 4-aza-5 α -androstan-3-one Steriods", *J. Org. Chem.* 58: pp. 3384 (1993).

Kitagawa, et al., "Structural Analysis of β -Turn Mimics Containing a Substituted 6-Aminocaproic Acid Linker", *J. Am. Chem. Soc.*, 117: pp. 5169-5178.

Klolic, "Amino Acids and Peptides LXXXIX Synthesis of L-4-Azalsine, D-4-Azalsine, and L-4-Azalsine- $[6-^{14}\text{C}]$ " *Coll. Czech. Chem. Comm.*, 34, pp. 630 (1969).

Kametani, et al., "A Simple Synthesis of 4-Thiazolidones, Tetrahydro-1,3-Thiazin-4-One and Hexahydro-1,3-Thiazepin-4-Ones from Amide-Thiols", *Heterocycles*, 9: pp. 831-840 (1978).

Krimm, "Uber Isonitron", *Chem. Ber.*, 91: p. 1057 (1958).

Krow, et al., "Regioselective Functionalization", *J. Org. Chem.*, 61: pp. 5574-5580 (1996).

Ksander, G.M., et al. "Dual Angiotensin Converting Enzyme/Thromboxane Synthase Inhibitors.", *J. Med. Chem.* 37: 1823-1832 (1994).

Kukolja, et al., "Orally Absorbable Cephalosporin Antibiotics", *J. Med. Chem.*, 28:12, pp. 1886 (1985).

Losse, G., et al., "Synthese Des Depsipeptides Valinomycin", *Tetrahedron*, 27, pp. 1423-1434 (1971).

Lowe, et al., "5,7-Diphenyl-3-Ureidohexahydroazepin-2-Ones as Cholecystikinin-B Receptor Ligands", *Bioorg & Med Chem Letters*, 4:24, pp. 2877-2882 (1994).

McKennis, et al., "The Synthesis of Hydroxycotinine and Studies on Its Structure", *Synthesis and Hydroxycotinine*", pp. 383-387 (1963).

Micouin, et al., "Asymmetric Synthesis", *Tetrahedron*, 52:22, pp. 7719-7726 (1996).

Miller, et al., "Application of Ring-Closing Methathesis to the Synthesis of Rigidified Amino Acids and Peptides", *J. Am. Chem. Soc.*, 118, pp. 9606-9614 (1996).

Mullan, et al., "A Pathogenic Mutation for Probable Alzheimer's Disease in the APP Gene at the N-Terminus of β -Amyloid", *Nature Genetics* 1, pp. 345-347 (1992).

Murrell, et al., "A Mutation in the Amyloid Precursor Protein Associated with Hereditary Alzheimer's Disease", *Reports*, pp. 97-99 (1991).

Nedenskov, et al., "Synthesis of Potential Hypnotics", *Acta. Chem. Scand.*, 12:7, pp. 1404-1410 (1958).

Ogliaruso and wolfe, *Synthesis of Lactones and Lactams*, Patai, et al., Ed., J. Wiley & Sons, NY:NY, (1993).

Orito, et al., "Benzolactams-1", *Tetrahedron*, 36:8, pp. 1017-1021 (1980).

Overberger, et al., "Optically Active Polyamides", *Brooklyn Polytechnic*, pp. 3431-3435 (1963).

Overberger et al., "The Synthesis of Optically Active C-Methyl-2-oxoheptamethyleminines and C-Methyl-7-aminoheptanoic Acids", *Macromolecules*, 1:1, pp. 1-6 (1968).

Parsons, et al., "Benzolactams. A New Class of Converting Enzyme Inhibitors", *Biochem. Biophys. Res. Comm.*, 117: pp. 108-113 (1983).

Pedersen, et al., "Studies on Organophosphorus Compounds", *Tetrahedron*, 35: p. 2433 (1979).

Reupple, et al., "Abberant Alkaloid Biosynthesis", *J. Am. Chem. Soc.*, 93: 7021 et seq. (1971).

Robl, et al., "Synthesis of Benzo-Fused, 7,5-and 7,6-Fused Azepinones and Conformationally Restricted Dipeptide Mimetics", *Tetrahedron Lett.*, 36:10, pp. 1593-1596 (1995).

Robl, et al., "Dual Metalloprotease Ihibitors", *Bioorg. Med. Che. Letter*, 4: pp. 1789-1794 (1994).

Rodriguez, et al., "Conformationally Restricted Analogues of Methionine", *Tetrahedron*, 52: pp. 7727-7736 (1996).

Sekakida, et al., "Studies on Seven-membered Heterocyclic Compounds Containing Nitrogen", *Bull. Chem. Soc. Japan*, 44: pp. 478-480 (1971).

Selkoe, et al. "Amyloid Protein and Alzheimer's Disease." *Scientific American*. 68-78 (1991).

Selkoe, et al. "The Molecular Pathology of Alzheimer's Disease." *Neuron*. 6:487-498 (1991).

Shirotu, et al., "Potential Inhibitors of Collagen Biosynthesis", *J. Med. Chem.*, 20: pp. 1623-1627 (1977).

Skiles, et al., "Eleastase Inhibitors Containing Conformationally Restricted Lactams", *Bioorg. Med. Chem. Letter*, 3: pp. 773-778 (1993).

Slusarchyk, et al., "Dual Metalloprotease Inhibitors.V.", *Bioorg. med. Chem. Lett.*, 5: pp. 753-758 (1995).

Smith, et al., "The Curtius Reaction", *Organic Reactions*, Ch. 9, pp. 337-449 (1946).

Suda, et al., "Metalloporphyrin-catalysed Rearrangement of Oxaziridines", *J. Chem. Soc. Chem. Comm.*, pp. 949-950 (1994).

Thomas, et al, "Nuclear Magnetic Resonance Studies and Conformational Analysis of Bicyclic Inhibitors of Angiotensin-converting Enzyme", *J. Chem. Soc. Perkin II*, 747 (1986).

Ugi, et al., "Ugi Reactions with Trifunctional α -Amino Acids, Aldehydes, Isocyanides and Alcohols", *Tetrahedron*, 52:35, pp. 11657-11664 (1996).

Van der Steen, et al., "Synthesis of 3-Amino-2-Azetidinones: A Literature Survey", *Tetrahedron Letters*, 47: pp. 7503-7524 (1991).

Vedejs, et al., "Synthesis of N-Methoxy and N-H Aziridines from Alenes", *Tetrahedron Letters*, 33: pp. 3261-3264 (1992).

Wada, et al., "Stereospecific and Stereoselective Reactions", *Bull. Chem. Soc. Japan*, 46: pp. 2833-2835 (1973).

Wasserman, et al., "Total Synthesis of (\pm)-Dihydroperiphylline", *J. Am. Chem. Soc.*, 103, p. 461-462 (1981).

Watthey, et al., "Synthesis and Biological Properties of (Carboxyalkyl)amino-Substituted Bicyclic Lactam Inhibitors of Angiotensin converting Enzyme", *J. Med. Chem.*, 28: pp. 1511-1516 (1985).

Wheeler, et al., "Formation and Photochemical Wolff Rearrangement of Cyclic α -Diazo Ketones", *Organic Syntheses*, Coll. Vol. VI, p. 840.

Wolff, "The Schmidt Reaction", *Organic Reactions*, ch. 8, pp. 307-336 (1946).

Yakoo, et al., "Studies on Seven-Membered Heterocyclic Compounds Containing Nitrogen", *Bull. Chem. Soc. Japan*, 29: p. 631 (1956).

Yanganasawa, et al., "Angiotensin-converting Enzyme Inhibitors", *J. Med. Chem.*, 30: p. 1984-1991 (1987).

Japanese patent application 179757 and published International Application No. WO 98/04539 have been cited merely for completeness of the record because both were cited by the Japanese examiner in the examination of the Japanese counterpart of the present application. Neither reference has an early enough effective reference date to be available as a reference against the present application. European patent application No. 810221A is the English language counterpart of International Application No. WO 96/25408, already of record herein. Due to problems encountered in downloading EP 810221A, the copy provided herein is missing pages 327-336.

The chemistry text, "The Synthesis of Lactose and Lactams" has been cited in an exercise of caution because it is referenced in the application as a synthesis resource. Because the text is over 1,000 pages, Applicants have merely enclosed the table of contents for the book.

A fee in the amount of \$180.00 (126) is enclosed in conformance with 37 C.F.R. § 1.97(c).

To assist the Examiner, the documents are listed on the attached form PTO-1449.
It is respectfully requested that an Examiner initialed copy of this form be returned to the undersigned.

Respectfully submitted,

BURNS, DOANE, SWECKER & MATHIS, L.L.P. ✓

^{JSFS}
Date: 9-4-02

By: Gerald F. Swiss
Gerald F. Swiss
Registration No. 30,113

P.O. Box 1404
Alexandria, Virginia 22313-1404
(650) 622-2300

RECEIVED
TECH CENTER 1600/2900
02 SEP -5 PM 4:34

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of

Jing Wu, et al.

Application No.: 09/916,440 ✓

Filed: July 30, 2001 ✓

For: CYCLOALKYL, LACTAM, LACTONE
AND RELATED COMPOUNDS,
PHARMACEUTICAL COMPOSITIONS
COMPRISING SAME, AND METHODS
FOR INHIBITING β -AMYLOID
PEPTIDE RELEASE AND/OR ITS
SYNTHESIS BY USE OF SUCH
COMPOUNDS

Group Art Unit: 1624

Examiner: B. Kifle

RECEIVED

SEP 12 2002

TECH CENTER 1600/2900

**SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT
TRANSMITTAL LETTER**

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

Enclosed is a Supplemental Information Disclosure Statement and accompanying form PTO-1449 for the above-identified patent application.

- ☐ No additional fee for submission of an IDS is required.
- ☒ The fee of \$180.00 (126) as set forth in 37 C.F.R. § 1.97(p) is also enclosed.
- ☐ A certification under 37 C.F.R. § 1.97(e) is also enclosed.
- ☐ A certification under 37 C.F.R. § 1.97(e), and the fee of \$180.00 (126) as set forth in 37 C.F.R. § 1.17(p) are also enclosed.
- ☐ Charge \$_____ to Deposit Account No. 02-4800 for the fee due.
- ☒ A check in the amount of \$ 180.00 is enclosed for the fee due.

The Commissioner is hereby authorized to charge any appropriate fees under 37 C.F.R. §§ 1.16, 1.17 and 1.21 that may be required by this paper, and to credit any overpayment, to Deposit Account No. 02-4800. This paper is submitted in duplicate.

Respectfully submitted,

BURNS, DOANE, SWECKER & MATHIS, L.L.P.

Date: 9-4-02
P.O. Box 1404
Alexandria, Virginia 22313-1404
(650)622-2300

By: Gerald F. Swiss
Gerald F. Swiss
Registration No. 30,113